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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	03/19/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 03/19/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/828,975	REN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-32 and 112-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *112 and 121* is/are allowed.

6)☒ Claim(s) *30-32,113-120 and 122-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendments submitted December 18, 2006 are acknowledged.

Claims 1-29 and 33-111 have been canceled

Claims 30-32 have been amended.

New claims 112-128 have been added.

Claims 30-32 and 112-128 are pending in the instant application.

Claims 30-32 and 112-128 are under examination in the instant office action as they read on CatSper2 polypeptides comprising the epitope species of amino acids 314-340 of SEQ ID NO:2. In view of the prior art, the species search has been extended to epitopes of SEQ ID NO:4.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 31 and 32 stand rejected and new claims 113-120 and 123-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record.

The office action mailed March 3, 2006 states:

> Applicant has claimed the genus of CatSper2 polypeptides and fragments thereof, and has disclosed the full length sequences of SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:6 as members of this genus. SEQ ID NO:2 and 4 appear to be human splice variants, while SEQ ID NO:6 is disclosed as mouse CatSper2. The specification defines the breadth of the term "CatSper2 protein" in paragraph 32 on page 32

wherein it is disclosed that CatSper2 proteins are sperm-specific cation channels and encompass SEQ ID NOs:2, 4, 6, allelic and splice variants of said SEQ ID numbers, and functional equivalents thereof. Note that allelic and splice variants and functional equivalents thereof reasonably include polypeptides 80% or more identical to SEQ ID NO:2, 4 or 6. The specification defines the activity of a CatSper2 protein to include induction of an ion current, mediation of Ca^{2+} influx, or the ability to complement the phenotype of CatSper2$^{-/-}$ sperm (see particularly paragraph 34 on page 11). Note that defining a protein by its ability to complement its absence is a circular argument that does not help a skilled artisan in identifying such a protein since one would already need to know the identity of the protein in order to generate the knockout cell line. Potential functional domains of CatSper2 are identified, such as transmembrane domains, pore region, and extracellular domains, based upon homology with known voltage-dependent ion channels (see particularly paragraphs 53, 54, 59, 60, and 179-182).

As indicated above, the term CatSper2 protein is broadly defined as being a sperm-specific cation channel. Such a definition reasonably indicates that other structurally distinct sperm- specific cation channel proteins, such as those disclosed by Ren et al. (reference AF on the IDS received March 31, 2005, see entire document, particularly Figure 1, (CatSper)) and Lobley et al. (Reprod Biol. Endocrinol. 2003, 1:53, see entire document, particularly Figures 1 and 2 (CatSper3 and CatSper4)) are encompassed by applicant's definition of a CatSper2 protein. The inclusion of variants and functional equivalents expands the breadth of the term even further, and applicant has claimed polypeptides that are 80% identical to a CatSper2 protein. Skolnick et al. (Trends in Biotechnology, 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate and often unpredictable, in part because of the multifunctional nature of proteins (see particularly the Abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two sequences, only experimental research can confirm the artisan's best guess as to the function of the structurally related sequence (see in particular the Abstract and Box 2 on page 36). The complexity of the problem of assigning function based on homology rises as the percent similarity or identity falls (see Whisstock et al., Quarterly Reviews of Biophysics, 2003, 36:307-340, particularly the sentence that spans pages 321 and 323).

It is noted that the specification teaches specific functional domains of CatSper2, such as transmembrane or pore regions, based upon homology with other known ion channels. However, it appears that when the CatSper2 proteins of SEQ ID NOs:2, 4, and 6 were expressed in multiple cell types, either alone or in conjunction with the related CatSper protein, no changes in current or ion flux could be observed (see particularly Example 10 of the instant specification, Quill et al. (reference AE on the IDS received 3/31/05, see entire document, particularly the paragraph spanning pages 12530-12531), and Lobley et al. (see particularly the abstract)). As such, there does not appear to be any evidence that the sequences identified by the specification as CatSper2 (i.e. SEQ ID NO:2, 4, and 6) actually function as sperm-specific cation channels. As such, it is not clear what functional activity a polypeptide 80% identical to SEQ ID NO:2, 4, or 6 would need to retain to be considered a CatSper2 polypeptide since the polypeptides of SEQ ID NO:2, 4, and 6 do not appear to have the disclosed functional property of being cation channels. Further note that the instant claims recite polypeptides that comprise only a portion or domain of a CatSper2 protein. Given that the full length proteins of SEQ ID NO:2, 4, and 6 do not appear to function as cation channels, polypeptides comprising only a portion or domain of said SEQ ID numbers certainly would not function as cation channels.

However, evidence does exist to indicate that CatSper2 is important for fertility since an infertile human patient has been identified who has a deletion in part of the CatSper2 gene located in chromosome 15q15 (Avidan et al., European Journal of Human Genetics, 2003, 11:497-502, see entire document). It is curious that the post-filing date art of Avidan et al. and the instant specification are discordant concerning the location of the CatSper2 gene, since the instant specification indicates that it resides on human chromosome 15q13 (see particularly paragraph 193 on page 59 of the instant specification). Therefore, while it is not certain that the polypeptides of SEQ ID NOs:2, 4, and 6 form functional cation channels, it is clear that the polypeptides of SEQ ID NO:2, 4, and 6 could be used to generate antibodies, said antibodies then being used to screen patients for infertility related to altered or defective expression of the proteins of SEQ ID NO:2, 4 or 6. Colman (Research in Immunology, 1994, 145:33-36) teaches that even single amino acid changes in an antigen can completely disrupt the binding between an antibody and an antigen (see particularly the paragraph that starts in the right column of page 33). As such, CatSper2 proteins that are less than 100% identical to the sequences of SEQ ID NO:2, 4, or 6 can elicit an antibody response wherein the elicited antibodies are not capable of binding to the wild-type CatSper2 proteins of SEQ ID NO:2, 4, and 6. The specification does not appear to disclose a utility for antibodies that cannot bind the wild-type CatSper2 sequences of SEQ ID NOs:2, 4, or 6, and as such the polypeptides that can be used to generate said antibodies do not appear to be enabled.

Therefore, given the breadth of the term "CatSper2 protein" as defined by the specification, the fact that the disclosed sequences of SEQ ID NO:2, 4, and 6 do not appear to act as cation channels as evidenced by Example 10 of the specification and the art of Quill et al. and Lobley et al., the fact that only experimental evidence can confirm functional similarity of sequences related by a given percent identity or homology as taught by Skolnick et al. and Whisstock et al., and the fact that while CatSper2 polypeptides can be used to generate antibodies, antibodies generated against sequences of less than 100% identity may not bind the wild-type sequence as taught by Colman and the specification does not appear to provide a use for antibodies that bind CatSper2 sequence other that those of SEQ ID NO:2, 4, and 6, and thus the polypeptides used to generate such antibodies also do not appear to have a disclosed use, a skilled artisan would not be able to make and use the full breadth of applicant's claimed invention without first conducting additional research.

Applicant's arguments filed December 18, 2006 have been fully considered but they are not persuasive. Applicant argues that polypeptides 80% identical to a CatSper2 polypeptide or fragments thereof are enabled because the specification teaches how to make and use such fragments to generate antibodies to detect mutant protein for diagnostic purposes.

This argument is not convincing because as stated in the rejection of record it is not clear what activity a polypeptide of 80% identity would comprise and thus it is unclear how a skilled artisan would use such a polypeptide. The use of 80% identical polypeptides to generate antibodies was discussed in the rejection of record, and as evidenced by the prior art of Colman (of record) antibodies raised to bind 80% identical sequences would not necessarily crossreact with the polypeptides of SEQ ID NOs:2, 4, and 6. While it appears that detection of CatSper2 expression levels may be informative in diagnosing infertility as taught by Avidan et al. (of record) there is no indication that polypeptides 80% identical to the recited SEQ ID numbers are diagnostic of infertility, and as such a skilled artisan would not reasonably make antibodies to such polypeptides.

Applicant also argues that the specification discloses numerous features and activities of "CatSper2" polypeptides in addition to ion channel formation and that example 10 is not evidence that CatSper2 polypeptides do not form ion channels.

This argument is not convincing because the other asserted activities such as "mediation of cAMP-induced Ca^{2+} influx, restoration of sperm motility when expressed in $CatSper2^{-/-}$ sperm and/or restoration of the ability to penetrate eggs when expressed in $CatSper2^{-/-}$ sperm" are utilities that are not supported by the disclosure of experimental evidence in the specification, and the only functional data supplied by the specification

indicates that CatSper2 does not form a functional ion channel. This observation was confirmed by Quill et al. (of record) who also failed to observe the formation of ion channels in the presence of additional, highly related ion channel polypeptides.

In Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005), the court states "[W]here there is "no indication that one skilled in [the] art would accept without question statements [as to the effects of the claimed drug products] and no evidence has been presented to demonstrate that the claimed products do have those effects," an applicant has failed to demonstrate sufficient utility and therefore cannot establish enablement" and "If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

Therefore, the examiner has focused attention on ion channel formation. It should also be noted that the title of the instant claimed invention is "Sperm-specific cation channel, Catsper2, and uses therefor" and as such the claimed polypeptides should presumably function as ion channels.

Applicant also argues that the examiner has mischaracterized the teachings of Skolnick et al. and Whisstock et al. (of record) to support the argument that sequence-based approaches to protein function are unpredictable.

This argument is not persuasive because while the references do indicate that sequence-based prediction is commonly used in the art, they teach that it is only a starting point and that additional methods are required to confirm the function of similar polypeptide sequences (i.e. ones that are not 100% identical, such as the recited genus of 80% identical polypeptides).

Applicant further argues that additional methods were used to characterize CatSper2 such as motifs, domains, expression and localization data as is disclosed in Figure 1, and Examples 3-5, 7, 8, and 10 of the instant application.

This argument is not persuasive because motif and domains are sequence-based methods (figure 1). Example 3 is cloning CatSper2 cDNA, which while providing an exact sequence does indicate function. Example 4 is a northern blot while example 5 is in situ hybridization, both of which demonstrate that mRNA is transcribed in a particular location but do not indicate what the gene does. Examples 7 and 8, immunoprecipitation and fluorescence immunolocalization indicate that the gene is expressed at the polypeptide level at certain locations, but there is still no indication of what the polypeptide does. Example 10 attempted electrophysiology measurements to test the hypothesis that CatSper2 is an ion channel, but the provided data does not support this hypothesis as being true. As such, the only techniques in addition to sequence-based predictions appear in Example 10, and this example does not demonstrate ion channel formation.

Applicant also argues that the specification teaches in paragraph 109 that "point mutations of a CatSper2 protein, however, can also cause infertility and can be detected with antibodies which are specific for epitopes including or affected by the mutant species."

This argument is not persuasive because applicant has not disclosed any mutants or mutant epitopes that are associated with infertility. As such there is no guidance or direction as to which 80% identical polypeptides are or are not associated with infertility. Without such guidance, a skilled artisan would need to engage in unpredictable trial and error research to determine if point mutations are indicative of infertility, and if so which mutations and their locations within a CatSper 2 polypeptide, before being able to make and use the instant invention.

For all of the above reasons, the rejection is maintained.

4. Claims 30 and 32 stand rejected, claim 31 as amended is rejected and new claims 113-120 and 122-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for the reasons of record.

The office action mailed March 3, 2006 states:

> Applicant has broadly claimed CatSper2 proteins, proteins comprising fragments of a CatSper2 protein, proteins 80% identical to a CatSper2 protein, and proteins containing fragments that are 80% identical to a CatSper2 protein. To support this genus, applicant has disclosed the proteins of SEQ ID NO:2, 4, and 6. Applicant has identified particular domains of CatSper2 based upon homology with other known cation channels. Skolnick et al. (Trends in Biotechnology, 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate and often unpredictable, in part because of the multifunctional nature of proteins (see particularly the Abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two sequences, only experimental research can confirm the artisan's best guess as to the function of the structurally related sequence (see in particular the Abstract and Box 2 on page 36). The complexity of the problem of assigning function based on homology rises as the percent similarity or identity falls (see Whisstock et al., Quarterly Reviews of Biophysics, 2003, 36:307-340, particularly the sentence that spans pages 321 and 323). As such, it is not clear that the domains identified by applicant actually have their disclosed functions. This is especially true since the full length proteins of SEQ ID NO:2, 4, and 6 failed to demonstrate the disclosed functional activities of induction of ion currents or mediation of Ca^{2+} transport when expressed by themselves or in conjunction with additional proteins as shown in Example 10 and the teachings of Quill et al. (reference AE on the IDS received 3/31/05, see entire document, particularly the paragraph spanning pages 12530-12531). As such, there does not appear to be any disclosed link between the structure of the molecule and its functional properties.
>
> The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3). As discussed above, the domains or regions of the claimed CatSper2 proteins that are critical for function and must be maintained are not defined by the specification, nor are regions that can be successfully modified without influencing function defined given that even the full length proteins of SEQ ID NO:2, 4, and 6 failed to demonstrate the functional characteristics of an ion channel when transfected into a cell. In light of this, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus of CatSper2 proteins, proteins comprising fragments of CatSper2 proteins, proteins 80% identical to a CatSper2 protein, and proteins containing fragments that are 80% identical to a CatSper2 protein. Thus, Applicant was not in possession of the claimed genus of all CatSper2 proteins, proteins comprising fragments of CatSper2 proteins, proteins 80% identical to a CatSper2 protein, and proteins containing fragments that are 80% identical to a CatSper2 protein. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant's arguments filed December 18, 2006 have been fully considered but they are not persuasive. Applicant argues that applicant's had possession of the instant claimed genus because the claims have been amended to recite polypeptides 80% identical to the entirety or to a portion of a CatSper2 polypeptide that is recited by SEQ ID number and that the specification teaches particular domains of CatSper2

polypeptides by reference to specific amino acid subsequences of SEQ ID NOs:2, 4, and 6.

This argument is not convincing because as was stated in the rejection of record, the full length polypeptides of SEQ ID NO:2, 4, and 6 do not appear to comprise functional activity as per the data supplied by applicant in the instant specification. Given that the full length polypeptides do not display functional activity, there cannot be a disclosed correlation between structure and function, and therefore any polypeptide comprising less than 100% identity with the full length polypeptides would not reasonably comprise the same functional activities as the full length polypeptides. Note that since the full length fragments do not appear to comprise a functional activity, fragments of these polypeptides also do not reasonably comprise functional activity. Note also that the structural domains and their associated functions that are asserted in the instant application for subsequences of SEQ ID NOs:2, 4, and 6 have been assigned by homology, a technique that is often incorrect as taught by Skolnick et al. and Whisstock et al. (of record).

Applicant also argues that the specification "does not demonstrate that CatSper2 lacks ion channel activity, but merely demonstrates "that CatSper2 alone does not form a functional ion channel in these cells".

This argument is not convincing because there is no demonstration that CatSper2 forms an ion channel, either in the instant specification or in the post-filing date reference of Quill et al. (of record) who were unable to form functional ion channels in the presence of additional polypeptides as was discussed in the rejection of record.

The rejection is maintained.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 118-120, and 126-128 are rejected under 35 U.S.C. 102(b) as being anticipated by Rosen et al. (WO 00/61624 A1, of record on the IDS received March 31, 2005, see entire document) for the reasons of record.

The office action mailed March 3, 2006 states:

> Rosen et al teach a polypeptide that is 100% identical to amino acids 108-350 of SEQ ID NO:2 of the instant invention (see entire document and the enclosed copy of the sequence search notes). Based upon the teachings in the specification found on pages 18-19 of the instant specification, the polypeptide taught by Rosen et al. comprises transmembrane domains, extracellular loops, a pore, and antigenic epitopes of a CatSper2 polypeptide. Note that the polypeptide of Rosen et al. encompasses the elected epitope of residues 316-340 of SEQ ID NO:2. It should also be noted that the definition of CatSper2 activity as defined in paragraph 34 found on page 11 includes activity as a calcium ion channel, and the polypeptide taught by Rosen et al. is disclosed to be a calcium channel expressed in human testes (see particularly pages 57 and 58 of Rosen et al.).
>
> Therefore, the prior art anticipates the claimed invention.

Applicant's arguments filed December 18, 2006 have been fully considered but they are not persuasive. Applicant argues that Rosen et al. do not teach the entirety of SEQ ID NO:2 and that none of the pending claims are drawn to sequences contained entirely within the Rosen et al. sequence.

This argument is not persuasive because applicant's claims do read on fragments that are contained entirely within the Rosen et al. sequence. Applicant has amended claims 30-32 to claim polypeptides that are not anticipated by the art of Rosen et al. and as such the rejection of these claims has been withdrawn. In addition to the amendments to previously pending claims applicant has also submitted new claims which are anticipated by the art of record.

Note that SEQ ID NO:2 and SEQ ID NO:4 of the instant application are 100% identical for the first 393 amino acids of the two polypeptides as demonstrated by the attached sequence alignment. Paragraph 60 of the instant application asserts structural domains of CatSper2 proteins, indicating that a pore region is amino acids 280-303 of SEQ ID NO:2/4 , with similar information being provided for transmembrane

domains (104-126, 146-166, 176-195, 206-288, 241-262, and 316-340 of SEQ ID NO:2/4) and extracellular loops (127-145, 196-205, and 263-315 of SEQ ID NO:2/4). As demonstrated by the provided alignment, the polypeptide disclosed by Rosen et al. is 100% identical to amino acids 108-350 of SEQ ID NO:2. As such, the polypeptide of Rosen et al. comprises "at least a transmembrane domain (note that it comprises 5 of the 6 recited in the specification)", "at least an extracellular loop (it comprises all 3 loop sequences disclosed)" and "at least a pore region" of SEQ ID NO:2 and SEQ ID NO:4 since SEQ ID NO:2 and 4 are identical at the residues recited in the instant claims. Note also that Rosen et al. teach that their polypeptide is an ion channel, one of the functional activities of CatSper2 polypeptides as taught in the instant specification.

Therefore, the prior art anticipates the claimed invention.

7. The following are new grounds of rejection necessitated by applicant's claim amendments received December 18, 2006.

8. Claims 30-32, 113-120, 123, 124, 126, and 127 are rejected under 35 U.S.C. 102(e) as being anticipated by Birse et al. (WO 01/90304 A2).

Birse et al. teach compositions comprising a polypeptide that is 99.8% identical to SEQ ID NO:4 of the instant application (see provided sequence alignment). Note that it is the same length as SEQ ID NO:4 of the instant application, and that it comprises at least transmembrane, pore and loop domain features of a CatSper2 protein, such as residues 280-303 of SEQ ID NO:4. Given that the full length polypeptide of SEQ ID NO:2 does not appear to comprise functional activity as is discussed in the rejections set forth under 35 USC 112, 1st paragraph, the polypeptide of Birse et al. would be able to complement the activity of an inactive mutant CatSper2 polypeptide. Further, the courts have stated:

> "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently

present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." Id.

Also note that the polypeptide of Birse et al. comprises amino acids 104-126 of SEQ ID NO:2, and that SEQ ID NO:2 and SEQ ID NO:4 of the instant invention are identical for the first 393 amino acids of the two polypeptides.

Therefore, the prior art anticipates the claimed invention.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 118 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the claim refers back to itself. As such the limitations encompassed by the claim cannot be known with certainty since circular reasoning is not logical.

11. Claims 112 and 121 are allowable.

12. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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